Connecting Vitamin D to Gene Expression in Pregnant African Americans

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Purpose: Vitamin D is a pro-hormone traditionally noted for its role in calcium homeostasis; however, it is increasingly being recognized for its role in gene expression (Hollis & Wagner, 2017). Vitamin D exerts its genomic influence by binding to and activating a high-affinity vitamin D receptor that acts as a gene transcription factor. This receptor is located on hundreds of genes, resulting in both direct and indirect regulation of upwards of 5% of the human genome (Hossein-Nezhad, 2013). This relationship implicates vitamin D as a potential regulator over multiple physiological processes integral to human health.

During gestation drastic changes in the metabolism of this hormone highlight the importance to both establishing and maintaining a vital pregnancy (Hollis & Wagner, 2017). Despite the vital importance of vitamin D, hypovitaminosis D is widespread with approximately one billion individuals deficient or insufficient worldwide (Bikle et al., 2017). In the United States (US), vitamin D deficiency is especially pronounced in the African American (AA) population which is reflected consistently across decades of data from the US National Health and Nutrition Examination Survey (Hilger et al., 2014). AA women also face numerous maternal health disparities that have also been associated with vitamin D deficiency, i.e. preterm birth and preeclampsia.

Vitamin D potentially plays a role in adverse maternal outcomes partly through the regulation of genes linked to physiologic processes that contribute to disease manifestation. In the US there is a racial/ethnic disparity in both vitamin D levels and the associated health outcomes for African Americans. The purpose of this study is to investigate the relationship between serum 25(OH)D vitamin D concentration and gene expression of peripheral blood in pregnant African Americans.

Methods: The current inquiry is a nested case-control study carried out utilizing a subsample from two ongoing studies at a research institution in the southeast United States on African American women and risk factors for preterm birth. Cases and controls will be selected from the women who have data for vitamin D (serum total 25(OH)D), gene expression (RNA), and key covariates including demographics,
season, and other nutritional indicators. This secondary analysis is approved by the respective institutional review board.

**Results:** Data will be analyzed prior to presentation using linear regression to test for associations between vitamin D concentration and differences in RNA expression. Subsequently, these vitamin D-linked genes will be used to determine enriched biological pathways.

**Conclusion:** The anticipated findings of this study should provide evidence of the association between serum vitamin D concentration and RNA expression patterns. Additionally, the results should reflect both novel and similar pathways previously identified in related studies. This data could uncover potential physiologic underpinnings for genomic and non-genomic role of vitamin D in maternal health outcomes. Evidence that serum vitamin D concentrations can contribute to changes in the transcriptome of pregnant women could have implications for supplementation, recommended dietary allowance, as well as screening protocols for at risk women. These results can also provide a predictive biomarker crucial for prevention and disease management, especially in those facing health disparities related to vitamin D deficiency.

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**Title:**
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**Keywords:**
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**Abstract Summary:**
Vitamin D potentially plays a role in maternal health outcomes partly through the regulation of genes linked to vital physiologic processes. This study investigates the relationship between serum vitamin D and gene expression in peripheral blood mononuclear cells of pregnant African Americans in the southeastern United States.

**References:**
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**Author Summary:** Sheila Jordan is a Labor, Delivery and Recovery nurse and current doctoral candidate at Nell Hodgson Woodruff School of Nursing. Her current research interests include chronic disease manifestations of pregnancy related hypertensive disorders, the role of nutrition in pregnancy outcomes, and exploring the influence of epigenetics on women’s health.

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**Author Summary:** Dr. Dunlop is a physician with decades of caring clinically for high risk populations of women and infants. She is also a well-respected researcher, focused on exploring the contribution of nutrition, the microbiome, metabolites, and chronic stress on preterm birth and adverse infant and family outcomes. Dissemination of her research has impacted maternal infant health worldwide.

Author Summary: Dr. Smith studies the role of genetic and environmental factors in the development and symptoms of stress-related disorders across the lifespan. She uses a number of complementary approaches including bioinformatics and genome-wide evaluations of sequence variants, DNA methylation and gene expression to explore developmental and behavioral problems.

Author Summary: Dr. Reilly is well published, a reviewer for several cardiovascular and critical care journals, and past-editor for AAHFN's Connection. She has been honored for her scholarship, teaching, and service with the Emory Williams Distinguished Teaching Award, induction as a Fellow of the American Heart Association, and the Heart Failure Society of America Nurse Investigator Award.

Author Summary: Dr. Tangpricha's research focus is translational research in areas of vitamin D nutrition, osteoporosis and cystic fibrosis. He is interested in the impact of vitamin D supplementation on extra-skeletal diseases such as hypertension and the immune system.